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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/101,423	11/27/1998	PHILIP S RUDLAND	WPT-0114-PUS	9634

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EXAMINER	
SHUKLA, RAM R	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 01/27/2003 27

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/101,423	Applicant(s) RUDLAND ET AL.	
	Examiner Ram R. Shukla	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-7,11,15-19,23 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *7 and 11* is/are allowed.

6)☒ Claim(s) *1,2,4-6,15-19,23 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The request filed on 6-04-02 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09101,423 is acceptable and a CPA has been established. An action on the CPA follows.

2. Amendment/Response filed 10-15-02 are acknowledged.

3. Amendments to claims 1, 6, 7 and 16 have been entered.

4. Non-elected claims 8-10, 12-14, 16, 20-22, and 24-28 have been cancelled.

5. As noted in the previous office action of 12-4-01, claims 1, 2, 4-7, 11,15-19, 23, and 29 pertaining to SEQ ID NO 4 are under consideration.

6. Objection to the specification for Compliance With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures is withdrawn.

7. Claim 16 is objected to because the term hybridization is misspelled.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 17 and 29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record set forth in the previous office action of 3-16-01 and 12-4-01.

Response to Arguments

Applicant's arguments filed 10-15-02 have been fully considered but they are not persuasive. It is noted that applicants have argued that since the met DNA

sequence is known and since method of oligonucleotides mediated modulation of mammalian gene expression are known and published an artisan could practice the claimed invention. Furthermore, applicants have listed several references and that these references are attached. However, these references were not part of the amendment or were filed in an IDS form. Accordingly, these references have not been considered. Even if these articles were present in the IDS form, the would not have been supported the enablement of the claimed invention because at the time of the invention, the method of treatment by targeting a sequence was not routine in the art and was unpredictable as discussed in the previous office action of 3-16-01 and 12-4-01. It is reiterated that several enablement issues were raised in the previous office actions of 3-16-01 and 12-4-01, regarding the unpredictability and undue experimentation of the clamed invention and the applicants have not addressed any of these issues. Furthermore, it is reiterated that the specification does not provide any guidance as to how the claimed medicament would have been prepared, what disease would have been treated, what doses would have been administered, and whether treatment of any disease would have been resulted after the administration of the claimed medicament . It is noted that the only description provided by the specification is on page 19 (last 6 lines) and page 20, which indicates that oligonucleotides could be used for blocking the expression the function of a regulatory DNA in a cancer. Applicants' argument that the claim is to a medicament not a method is not persuasive because the intended use of the medicament is for treatment and the composition has to be enabled for the intended use. Therefore, the enablement rejection is maintained for the reasons of record set forth in the previous office actions of 3-16-01 and 12-4-01.

10. Claims 1-2, 4, 5, 18, and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed method wherein a fragment of human DNA of less than 1.5 kb in length, wherein said human DNA is obtained from malignant, metastatic cancer cells, wherein said fragment of human DNA is tagged at both ends with double-stranded synthetic oligonucleotides, and wherein said double stranded oligonucleotides provide

restriction enzyme and unique PCR primer sites, is transfected into rat mammary epithelial cells, Rama 37, transformed Rama 37 cells are injected into mammary glands of rats, rats injected with transformed Rama 37 cells are selected in which metastasizing tumors have been identified, and the regulatory DNA that induces metastasis are isolated and recovered from the metastasis tissue of the rats, does not reasonably provide enablement for other claimed embodiments for reasons of record set forth in the previous office action of 3-16-01 and 12-4-01. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Response to Arguments

Applicant's arguments filed 10-15-02 have been fully considered but they are not persuasive. Applicants argue, "The whole essence of the application is that the fragments have to be of the specific sequence as indicated". However, it is not clear as to what is that specific sequence. The claim 1 does not recite any specific sequence rather it recites a sequence of less than 1.5 KB isolated from a malignant, metastatic cancer cells and therefore, the question is: what is the specific sequence? It is reiterated that the office action discussed the enablement based on sound scientific reasoning and applicants have not addressed these issues as set forth in the office action of 3-16-01. Applicants' argue that the individual methods were standard in the art and cite Davies et al, however, Davis et al only teaches that a method using Rama37 cells and not any other cell line that forms a benign tumor. It is noted that applicants have not described any other cell line that produces a benign non-metastasizing tumor when injected in a syngeneic animal. Applicants have neither provided any evidence nor described any other cell line that produces benign and non-metastasizing tumor when injected in a syngeneic animal and which when transfected with another DNA will produce metastasis. Therefore, an artisan of skill would not have known how to decide which cell line will produce only benign non-metastasizing tumor in a syngeneic animal and the neither the art

of record nor the specification describes what such a cell line will be what will be its characteristics and structure. Therefore, the enablement rejection is maintained.

11. Claims 1-2, 4, 5, 18 and 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claimed invention is directed to a method of identifying screening and recovery of a regulatory DNA that is not expressed as an mRNA but is capable of inducing metastasis, said method comprising transferring a cell line that produces only benign non-metastasizing tumors when injected in a syngeneic animal, injecting transformed cells into the syngeneic animal, selecting animals with metastasizing tumors and recovering the regulatory DNA.

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. When the claims are analyzed in light of the specification, instant invention recites a genus, a cell line. The specification only teaches a rat mammary epithelial cell line Rama37. The specification does not teach any other member of the genus.

Next, then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e. other than nucleotide sequence), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case, the only other identifying characteristic is that the cell line produces only benign non-metastasizing tumors when injected in a syngeneic animal. The specification does not disclose any identifying characteristic as to how an artisan would have differentiated one species of the genus from another species of the genus.

Applicants' attention is directed to the decision in *In re Shokal*, 113 USPQ 283 (CCPA 1957) wherein is stated:

It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

Accordingly, this limited information is not deemed sufficient to reasonably convey to one skilled in the art that the applicant is in possession of the broad genus of the modulators or agents at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed genus.

12. Claim 16 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is drawn to a kit for diagnosing the likelihood of a cancer metastasizing comprising any probe that specifically hybridizes to the DNA of SEQ ID NO 4, color indicator, oligonucleotides primer, material for gel analysis and DNA transfer and hybridization. However, the specification as filed is not enabling for the claimed invention because the specification does not provide any guidance as to how will a probe be designed, what will be its length and other characteristics so that it does not hybridize with any other DNA but with the DNA of SEQ ID NO 4. For example, the nt 827-844 of Sasaki et al ((US 5808024, 9-15-1998, filing date 6-7-1995) has 100% sequence identity with 17 nucleotides of SEQ ID NO 4 and therefore, it will specifically hybridize to SEQ ID NO 4 as well as the nucleic acid of Sasaki et al. However, the presence of DNA of Sasaki et al is not indicative of the cancer metastasizing. Therefore, using a probe that specifically hybridizes to SEQ ID NO 4, an artisan could not specifically identify SEQ ID NO 4

and not be able to use the claimed kit for intended use. The specification as filed does not provide sufficient guidance as to how an artisan of skill would have designed and use a probe that will be specific to SEQ ID NO 4 and would not hybridize to any other nucleic acid sequence.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 1, 2, 4-6, 15, 17-19, 23, and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the transformed cells" in step (ii). There is insufficient antecedent basis for this limitation in the claim since a transformed cell has not been recited in step (i).

Claims 2, 4-6, 15, 17-19 23 and 29 are indefinite as they are dependent on claim 1.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

16. The 102 rejection in view of Chen et al has been withdrawn.

17. Claims 15 and 23 are rejected under 35 U.S.C. 102(e) as being anticipated by Sasaki et al (US 5808024, 9-15-1998, filing date 6-7-1995) for reasons of record set forth in the previous office action of 12-4-01.

Response to Arguments

Applicant's arguments filed 10-15-02 have been fully considered but they are not persuasive. It is noted that the claimed invention is directed to a probe that is specific to a DNA, the nt 827-844 of Sasaki et al meets the limitation of the claimed composition. Applicants arguments that the cited art does not teach means to design specific probe is not relevant since the nt 827-844 of Sasaki et al have the same structure as the claimed probe and therefore they will be specific to a DNA that will have these nucleotides.

18. Claims 7 and 11 drawn to a regulatory DNA comprising the sequence of SEQ ID NO 4 are free of the prior art of record.

When amending claims, applicants are advised to submit a clean version of each amended claim (without underlining and bracketing) according to § 1.121(c). For instructions, Applicants are referred to http://www.uspto.gov/web/offices/dcom/olia/aipa/index.htm.

Applicants are also requested to submit a copy of all the pending/under consideration claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this

application or proceeding should be directed to the William Phillips whose telephone number is (703) 305-3413.

RAM R. SHUKLA, PH.D
PATENT EXAMINER

Ram R. Shukla, Ph.D.
Primary Examiner
Art Unit 1632